Amendments to the Claims

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1-7. (Cancelled)

8. (Currently Amended) A method for designing an antisense oligonucleotide sequence for a target mRNA or its precursor, the method comprising the steps of:

~~(a) selecting all pairs of sequences on the target mRNA, or its precursor, complementary to each other and separated by at least three nucleotides, but without independently selecting pairs of sequences which are shorter than, and composed of nucleotides of, the selected sequences;~~

(a) selecting a first sequence of a pair of sequences, the first sequence consisting of 2 or more nucleotides from the target mRNA or its precursor;

(b) selecting a second sequence of a pair of sequences, wherein the second sequence is complementary to the first sequence and is separated by at least three nucleotides from the first sequence;

(c) examining whether the lengths of the first and second sequences can be extended to include neighboring nucleotides by checking for complementarity between corresponding single nucleotides neighboring the terminal nucleotides of each of the first and second sequences;

(d) when complementarity is found in step (c), extending the lengths of each of the first and second sequences by one nucleotide resulting in intermediate first and intermediate second sequences, wherein the one nucleotide on the intermediate first

sequence and the one nucleotide on the intermediate second sequence are the corresponding nucleotides checked for complementarity in step (c);

(e) repeating steps (c) and (d) in both directions of the intermediate first and intermediate second sequences until complementarity is not found;

(f) determining the nucleotide sequences of the final first and final second sequences resulting from performing steps (c) through (e);

[[(b)]] (g) ~~assigning~~ obtaining a numerical value ~~to~~ for ~~each~~ the pair of final first and second sequences, [[that]] wherein the numerical value reflects the possibility of forming a complementary double-stranded region between said pair of final sequences based upon the distance between said pair of final sequences and the bond energy ΔG for said pair of final sequences, wherein a lower numerical value indicates a lower possibility, and wherein the numerical value increases with an increase in said bond energy and the value decreases with an increase in the distance between said paired final sequences;

[[(c)]] (h) assigning the numerical values obtained in step [[(b)]] (g) to each nucleotide ~~of each~~ of the paired final sequences;

(i) with the same first sequence already selected as in step (a) and starting at a different second sequence from that already selected in step (b), repeating steps (b) through (h) until all complementary second sequences for said first sequence have been selected;

(j) repeating steps (a) through (i) for all possible first sequences on the target mRNA or its precursor without selecting the same pair more than once;

[[(d)]] (k) summing the numerical values, which are assigned in step [[(c)]] (h) for all pairs of final sequences selected in steps (a) to (j), for each nucleotide in the target mRNA or its precursor;

[[(e)]] (l) selecting one or more regions each of which consists of at least 6 contiguous nucleotides and has a low summed numerical value relative to the summed numerical value of another region; and

[[(f)]] (m) designing one or more antisense oligonucleotides, wherein each antisense oligonucleotide is complementary to ~~a region~~ one of the one or more regions selected in step [[(e)]] (l).

9. (Previously Presented) The method of claim 8, wherein said bond energy for forming the complementary double-stranded region is determined by the nearest neighbor model.

10. (Cancelled)

11. (Previously Presented) The method of claim 8, wherein said numerical value is expressed as $((L+1)/r)^F \cdot \exp(|\Delta G|/RT)$, wherein ΔG is the bond energy for forming a complementary double-stranded region, R is the gas constant, T is the absolute temperature, L is an integer from 3 to 10, r is one plus the number of nucleic acid bases between said first target region and said complementary region, with the provision that $r \geq L+1$, and F is a positive number not greater than 6.

12. (Previously Presented) The method of claim 11, wherein $|\Delta G|$ is determined by the nearest neighbor model.

13. (Previously Presented) The method of claim 11, wherein L is 4 to 6.

14. (Previously Presented) The method of claim 11, wherein L is 4.

15. (Previously Presented) The method of claim 11, wherein F is 6.

16. (Previously Presented) The method of claim 11, wherein L is 4 to 6, and $|\Delta G|$ is determined by the nearest neighbor model.

17. (Previously Presented) The method of claim 11, wherein L is 4, and $|\Delta G|$ is determined by the nearest neighbor model.

18-25. (Cancelled)